REMARKS

The Applicants thank the Examiner for his helpful suggestions during the telephone interview of April 21, 2004. The topics discussed included possible amendments to claim 29.

Please cancel withdrawn claims 17-28 without prejudice or disclaimer of the subject matter thereof. Claims 29–34 and 36-42 are pending.

First Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner has maintained the rejection of claims 29-34 and 36-42 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement.

In the original rejection in this regard (mailed 5/7/03), the Examiner stated that the p27 gene was not described in the specification in a manner to reasonably convey to the skilled artisan that Applicants had possession thereof at the time of filing. More particularly, the Examiner stated that the "instant claims and specification only provide a description for a species of cDNA which encodes only the transcribed region of the p27 protein" and that "a gene is a genus which comprises non-transcribed control regions both 5' and 3' to the transcribed region."

In originally responding, Applicants believed it was important to point out that the specification recognized and described regulatory elements for use with the p27 coding sequence but did not intend for the term "gene" to be used in any other manner than its standard form of usage. If Applicants' use of "gene" was unclear in the last response or has been misapprehended by the Examiner, Applicants regret the confusion. Throughout

the specification and current claims, Applicants use the word "gene" in the manner ascribed to its standard usage in the art and do so not only with respect to p27 genes but also for the other genes mentioned in the specification. Applicants respectfully note that skilled artisans commonly use the word gene as a shorthand for the protein coding sequence, for cDNA or for the genomic sequence as well as for any of these sequences in conjunction with naturally-associated or heterologous regulatory or other elements of the gene in question.

Applicants respectfully submit that having a clone and knowledge of the coding sequence for a gene product is sufficient to evidence possession of that "gene" in expressible form. In this context, knowledge of the exact identity of the naturally-associated regulatory elements of a gene is not necessary since many regulatory elements and expression vectors (with the necessary regulatory elements for expression of cDNA or genomic sequences) are well known in the art.

Accordingly, identification of the coding sequence for p27 is sufficient to evidence possession of a gene encoding p27, particularly in this case where the claims are not directed to the p27 gene *per se*, but rather are directed to a combination of a catheter and the p27 gene.

With respect to the written description, Applicants' specification not only provides such information for one species of p27 (murine), but also provides the coding sequences for human and mink p27. Applicants draw the Examiner's attention to the specification at page 7, line 19 to page 8, line 1, which indicates that the nucleotide and amino acid sequence of murine p27 is set forth in the specification in Fig. 5 as well as in SEQ ID NO. 2. This passage also states that "cDNAs encoding p27 are described by

PCT Publication No. WO95/18824, PCT Publication WO96/02140 (Applicant: Sloan-Kettering Institute For Cancer Research), Toyoshima *et al.* (Cell 1994, 78:67-74) and Polyak *et al.* (Cell 1994, 78:59-66)."

The two PCT publications reveal that the cDNA for human, mouse and mink p27 had been isolated and provide the amino acid sequences thereof (see, Figs. 9A and B in WO95/18824 and WO96/02140).[1] Additionally, WO96/02140 provides the nucleotide and amino acid sequence for mink, mouse and human cDNAs encoding p27 (Figs. 13-15, respectively). Toyoshima and Polyak report the cloning and expression of murine p27—indicating that those of skill in the art were in possession of a p27 gene in a form that allowed its expression at the time the present application was filed. Similarly, WO96/02140 reports recombinant expression of the murine p27 coding sequence under control of the CMV promoter—that is, recombinant expression of a p27 gene (page 68, e.g., Table III). Finally, the present application provides multiple constructs that comprise a p27 gene—here with the p27 gene under control of the CMV promoter (Figs. 2-4).[2] Given that genetic regulatory elements were well known to those of skill in the art at the time of filing, that the coding sequence for p27 from three different species was known at the time of filing, and that those of skill in the art could readily obtain a p27 genomic clone based on this information, Applicants believe the specification provides more than a sufficient written description to evidence that Applicants were in possession of genes encoding p27 in an expressible form at the time of filing.

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[1] Descriptive material for these Figs. 9A and 9B is found in WO95/18824 at pages 16 and 65-66 and in WO96/02140 at pages 16 and 66-67. Both PCT publications were published prior to the earliest filing date of the present application.

[2] As an aside, these same figures show plasmids encoding the tk gene product under regulatory control of the CMV promoter, *i.e.*, "a tk gene," as embraced by Claim 29 which recites that the "nucleic acid further comprises a gene encoding a cytotoxic agent." The Examiner has not indicated such genes lack written description support.

Additionally, there is no requirement or limitation in the present claims that the regulatory elements be those naturally associated with the p27 gene. In fact, the specification expressly states that different regulatory elements, e.g., promoters, enhancers, polyA signals can be used (page 9, line 4 to page 10, line 14).

Accordingly, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

Second Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner rejected Claims 29-34 and 36-42 under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description requirement because of new matter, and in particular for failure to describe any combination of catheter with a nucleic acid other than a balloon catheter.

In response, Applicants have amended claims 29-31 to recite that the catheter is a balloon catheter. The amendments are supported, *inter alia*, by the specification at page 12, lines 16-17 which states that the "compositions of the present inventions are preferably administered . . . by balloon catheter implantation into the blood vessel wall, such as described in U.S. 5,328,470." The '470 patent describes both double balloon (Fig. 1; col. 7, lines 2-18) and single balloon catheters (Fig. 2; col. 8, lines 36-46). Since the '470 patent is incorporated in the specification by reference (as stated at page 31, lines 5-6), Applicants submit that these amendments do not present new matter and have thus overcome this rejection under 35 U.S.C. §112, first paragraph. Accordingly, withdrawal thereof is respectfully requested.

Conclusions

For all the foregoing reasons, Applicants believe this application is in condition for allowance and early notice to this effect is earnestly solicited. If, for any reason, the Examiner is unable to allow the application and feels that an interview would be helpful to resolve any remaining issues, he is respectfully requested to contact the undersigned attorney at (312) 321-4229.

Respectfully submitted,

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